

REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 168-187 are in the case. Claims 188-189 are cancelled without prejudice.

I. CLAIM OBJECTIONS

Claim 179 has been objected to because it recites a different structure than was previously presented in claim 153. In response, claim 179 has been amended to recite the structure shown in claim 179 as presented in the Amendment dated March 21, 2008. Similar revisions have been made to claims 180-183, 185 and 186. It is believed, therefore, that these claims should not be "withdrawn from consideration". Reinstatement of claims 180-186 to consideration status is accordingly respectfully requested.

II. THE 35 U.S.C. §112, FIRST PARAGRAPH, REJECTION

Claims 168-179 and 187-189 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement, on the ground that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection then immediately goes on to discuss lack of enablement and the factors which may be considered in reaching a determination with respect to lack of enablement. Thus, the Action states:

"... while being enabling for the use of the particular constructs B_{tr}-sp-Ad-DOPE, A_{tr}-sp-Ad-DOPE, H_{tr}-sp-Ad-DOPE, A_{tr}-spsp₁-Ad-DOPE, A_{tr}-sp-Ad-DSPE for incorporation into the lipid bi-layer of a cell, [the specification] does not reasonably provide enablement for the use of any construct of the formula F-S₁-S₂-L wherein F is a glycotope for the same, and does not reasonably provide enablement for effecting any change in the surface antigens expressed by a cell." (Emphasis in the original)

It is unclear, therefore, whether the rejection is one of alleged lack of written description, or one of alleged lack of enablement. Both will be considered and are traversed.

The specification (page 18, lines 37 onwards) states:

"The inventors have determined that to prepare synthetic molecule constructs of the invention where the antigen (F) is an oligosaccharide selected from the group of glycotopes for A-, B- and H-antigens of the ABO blood groups, the primary aminoalkyl, secondary aliphatic aminoalkyl or primary aromatic amine, and the activator should be selected to provide a spacer (S₁-S₂) with a structure according to one of those presented below:

Alternative structures of S ₁ -S ₂ for a water soluble synthetic molecule construct (F-S ₁ -S ₂ -L) where F is a carbohydrate (or other antigen) with similar physico-chemical properties to the carbohydrate portion of the A-, B- or H-antigens of the ABO blood groups and L is a glycerophospholipid (n, m independently = 2 to 5)	
S ₁ is selected from:	S ₂ is selected from:
-O(CH ₂) _n NH-	-CO(CH ₂) _m CO- or -CO(CH ₂) _m NHCO(CH ₂) _n CO-

The specification further states (page 19, lines 3 to 6):

"It will be understood by one skilled in the art, that once the structure of the spacer (S₁-S₂) has been determined for a given class of antigens, the same structure of the spacer can be adopted to prepare synthetic molecule constructs of other classes of antigen with similar physico-chemical properties."

The particular constructs disclosed in the specification comprise a mono-, di-, tri- or oligosaccharide. The Action accepts that the specification is "enabling" for the use of the particular constructs disclosed in the specification where the antigen is a mono-, di-, tri- or oligo- saccharide.

In light of this, and without conceding to the rejection, claim 168 has been amended to be directed to a method of incorporating a synthetic molecule construct of the structure F-S₁-S₂-L into the lipid bi-layer of a cell or a multi-cellular structure comprising the step of contacting a suspension of the cell or multi-cellular structure with the synthetic molecule construct for a time and at a temperature sufficient to allow incorporation where F is a mono-, di-, tri- or oligo- saccharide; S₁ is 2-aminoethyl, 3-aminopropyl, 4-aminobutyl, or 5-aminopentyl; S₂ is -CO(CH₂)₂CO-, -CO(CH₂)₃CO-, -CO(CH₂)₄CO- or -CO(CH₂)₅CO-; and L is a diacyl- or dialkyl- glycerophospholipid.

The invention as claimed is clearly supported by an adequate written description. Moreover, it would have been understood by one of ordinary skill in the art as of the filing date of the case that mono-, di-, tri- and oligosaccharides have similar physico-chemical properties and could be substituted for those comprised in the particular constructs disclosed. It is believed, therefore, that the method as now claimed is also supported by an enabling disclosure, and could have been carried out by one of ordinary skill as of the filing date of the application without the exercise of undue experimentation.

Thus, in regard to the various "Wands" heading appearing in the Action, referring to the heading directed to the nature of the invention and the breadth of the claims, it is stated at page 34, lines 36 to 38 of the specification:

"As described herein not all structures of the spacer (S_1 - S_2) will provide a synthetic molecule construct (F - S_1 - S_2 - L) that is water soluble and spontaneously and stably incorporates into a lipid bi-layer such as a cell membrane."

The breadth of the claims is directed to the use of synthetic molecule constructs comprising the substructure S_1 - S_2 that have been demonstrated or reasonably predicted to have the favorable combination of characteristics. The claims as amended are drawn to a method of incorporating a synthetic molecule construct into the lipid bi-layer of a cell or multi-cellular structure. The synthetic molecule constructs as defined in the claims are water soluble, yet spontaneously and stably incorporate into the lipid bi-layer of a cell or multi-cellular structure. By virtue of this combination of characteristics, the synthetic molecule constructs are biocompatible and preclude the requirement to use detergents or organic solvents. Use of the synthetic molecule constructs defined in the claims allows the level of expression of an oligosaccharide at the surface of a cell or multi-cellular structure to be introduced or increased without loss of vitality of the cell or multi-cellular structure. The advantages of the invention are discussed in detail at page 17, line 16 onwards of the specification as published.

Referring to the heading relating to the state of the prior art and the predictability or unpredictability of the art, the Action states:

"As mentioned in the instant specification, insertion of GPI linked protein into membranes is known."

This prior art is of little if any relevance to the preparation and use of synthetic molecule constructs as defined in the claims as amended. This prior art does not impact on enablement of the invention as claimed.

With regard to the heading directed to the amount of direction or guidance presented and the presence or absence of working examples, the Action states:

"... the invention is understood to involve insertion of the claimed constructs into a cell membrane, which would increase the number of antigens or possibly add any new antigen that was previously absent."

The claims as amended define a method that would increase or possibly add a level of expression of a mono-, di-, tri- or oligo- saccharide antigen. On reading the claims as a whole, the original phrase "effecting... changes in the surface antigens expressed by the cell" would have been understood by one of ordinary skill to mean changes that resulted in an increase or addition. Notwithstanding this, the claims as amended refer to incorporating a synthetic molecule construct and any ambiguity arising from a partial reading of the claim (it is believed that no such ambiguity existed previously or presently exists) is now excluded.

The Action states:

"The specification (page 52, table 22) also states that, of only nine exemplary constructs, Gal β -sp-Ad-DOPE (IX) and H $_d$ -sp-Ad-DOPE (VIII) were not suitable for use in the transformation of cells because the glycotope was not recognised."

The Action further states:

"Given that two of the five glycotopes in this very small sampling of the entire scope of claim 168 are not suitable for use in the transformation of cells, the skilled artisan would not expect the entire scope of claimed constructs to be effective."

This latter statement is not correct. It appears that the statement may arise from a misunderstanding of the data presented in Table 22. The transformation ability of the

synthetic glycolipids presented in Table 22 is assessed by the agglutination of red blood cells. This agglutination is mediated by antibodies. If no reactivity occurs between the antibodies used and the incorporated antigens, then no agglutination will occur. As stated in the legend to Table 22:

"The lack of detectable transformation for Gal β -sp-Ad-DOPE (IX) and H α -sp-Ad-DOPE (VIII) was thought to be due to the inability of the antibody to recognise the glycotope of these synthetic molecules."

The inability to detect transformation of red blood cells by the synthetic molecule constructs identified in the Action is attributable to no reactivity between the antibody and the incorporated antigens (Gal β or H α) (F) of these constructs as opposed to an inability to incorporate.

With regard to the heading relating to the quantity of experimentation necessary, in light of the substantial guidance provided in the specification, one of ordinary skill in the art would have had to perform little, if any, additional experimentation to practice the invention commensurate in the scope with claimed invention. No undue experimentation issues arise with regard to the claimed invention.

In the Response to Arguments section, the Action states:

"The applicant argues that the construct of the claimed genus can be prepared by reaction of an activated lipid and an aminoalkyl glycoside as exemplified in the specification. However, as discussed above, the full scope of which glycosides are suitable, how to determine their suitability, and how to prepare them is not taught in the specification."

In response, the specification provides adequate teaching to one of ordinary skill of which glycosides are suitable. An aminoalkyl glycoside of a mono-, di-, tri- or oligosaccharide would be suitable. Thus, it is not correct, as asserted on page 8 of the

Action, that two of five glycotopes exemplified by the applicant were shown not to be effective.

The inclusion of the phrase "a solution of" in respect of the synthetic molecule construct in the claimed method yet further defines the subject matter which the applicants regard as their invention. Support appears at page 17, line 16 to 18 of the specification, where it is stated:

"The synthetic molecule constructs of the invention spontaneously and stably incorporate into a lipid bi-layer, such as a membrane, when a solution of the molecule is contacted with the lipid bi-layer." (Emphasis added).

Further support appears at page 17, lines 21 to 22 of the specification, where it is stated:

"Surprisingly, the synthetic molecule constructs identified herein have also been found to be water soluble."

Based on the above, it is clear that the presently claimed invention is supported by an adequate written description as well as an enabling disclosure. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

III. THE 35 U.S.C. §112, SECOND PARAGRAPH, REJECTION

Claims 168-179 and 187-189 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Action asserts that claim 168 and dependent claims 169-174, 177, 178, and 187-189 are drawn to the use of a synthetic molecule construct of the structure F-S₁-S₂-L, wherein F is a glycotope.

and that the specification states that "glycotope" is the antigenic determinant located on the carbohydrate portion of a glycolipid. The Action asserts that the specification does not define which portions of which glycolipids are suitable, thereby allegedly making it impossible to determine the metes and bounds of the claims with respect to the variable F.

Claims 188 and 189 have been canceled without prejudice. The rejection insofar as it relates to those claims is accordingly rendered moot.

In response, the term "glycotope" as the definition of the structural limitation F of the synthetic molecule construct F-S₁-S₂-L has been replaced by the phrase "mono-, di-, tri- or oligo- saccharide". Support for this amendment is provided by the embodiments of the synthetic molecule constructs described in the specification where each comprises a mono-, di-, tri- or oligo- saccharide. The definitions of the other structural limitations (S₁, S₂ and L) of the synthetic molecule construct (F-S₁-S₂-L) defined in claim 168 have been amended for consistency. Thus, the options for S₁ to be 2-aminoethyl and S₂ to be -CO(CH₂)₂CO- have been introduced. Support for these options appears in the Table at page 19 of the specification.

The Action further asserts that claim 168 and dependent claims 169-179 and 187-189 are drawn to a method of effecting change in the surface antigens expressed by a cell or multi-cellular structure, but that the specification allegedly does not define the changes that are effected. The Action notes that the specification does state that one object of the invention is to incorporate the F-S₁-S₂-L molecule into the lipid bilayer of a cell, but takes the position that that is not a definition of the allegedly vague and

indefinite recitation "effecting change in the surface antigens expressed by a cell or multi—cellular structure."

In response, and without conceding to the rejection, the phrase "effecting change in the surface antigens expressed by" in the preamble of claim 168 has been replaced by the phrase "incorporating a synthetic molecule construct of the structure F-S₁-S₂-L into the lipid bi-layer of". Support for this amendment appears at page 2, lines 31 to 33 of the specification as published (Publ. No. WO 2005/090368).

No new matter is entered and no new issues are raised in the currently amended claims. Entry and favorable considered are respectfully requested.

Favorable action is awaited.

Respectfully submitted,

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